

## Using the LLNA to Categorize Strong Skin Sensitizers

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According to the U.S. Bureau of Labor Statistics, allergic contact dermatitis (ACD) is one of the most common types of occupational disease. Because the prognosis of ACD is poor, prevention is imperative. Criteria have recently been adopted to distinguish strong sensitizers from other sensitizers based on human, guinea pig, and LLNA data. Substances with positive responses in the human maximization test (HMT) or human repeat insult patch test (HRIPT) at induction thresholds  $\leq 500 \mu\text{g}/\text{cm}^2$  are classified as strong sensitizers. Similarly, LLNA EC3 values  $\leq 2\%$  are proposed to categorize substances as strong sensitizers and LLNA EC3 values  $>2$  to categorize substances as “other sensitizers”. In order to evaluate the accuracy of the LLNA for identifying strong sensitizers as defined by human data, NICEATM and ICCVAM used a database of 112 substances with both LLNA and human data to calculate human potency classification categories (strong vs. other than strong) predicted by various EC3 values. Classifications based on EC3 values were compared to those defined by several different threshold values derived from HMT and HRIPT studies. Based on the available database, 64% of strong human sensitizers were correctly predicted using LLNA EC3  $\leq 2\%$ , while the remaining 36% of strong sensitizers were underclassified as “other sensitizers”. The current database indicates that over 1/3 of strong sensitizers would be underclassified as weaker skin sensitizers if the LLNA is used to determine potency categories. The LLNA should not be considered as a stand-alone test to predict skin sensitization potency. The LLNA EC3  $< 2\%$  can be used to categorize a substance as a strong sensitizer. However, substances with EC3 values greater than 2% are not necessarily moderate or weaker sensitizers. The LLNA should be used in an integrated decision strategy (e.g., with QSARs, peptide reactivity, human evidence, and historical data from other animal studies) to discriminate between strong and other skin sensitizers. ILS supported by NIEHS contract N01-ES-35504.

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Categories: Regulatory/Policy (Hypersensitivity - 2nd choice)